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# STRUCTURES OF TWO OXIDATION PRODUCTS OBTAINED FROM PALYTOXIN

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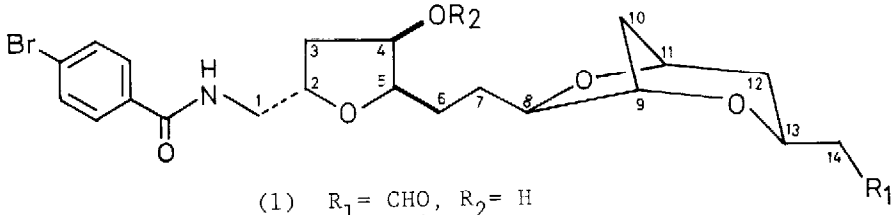
Summary: The structures of two oxidation products of N-(p-bromobenzoyl)palytoxin were unambiguously determined by means of X-ray crystallographic analysis.

In our previous papers,[1,2] we reported the structures of the products obtained by the treatment of N-acetylpalytoxin with $NaIO_4$ on polystyrene gel column. Among those, two series of compounds could be assigned as the moieties containing the terminal amino group and the most lipophilic part, respectively, in palytoxin. In order to determine the structures of two series of compounds, we attempted the X-ray crystallographic analysis. Especially, we believe that the structure determination of this nitrogen-containing segment will lead us to the elucidation not only of the full structure of palytoxin but of its structure-toxicity relationship because the toxicity of this toxin may depend on this terminal amino moiety.[1] We wish to describe partial structures of palytoxin in this report.

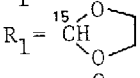
Oxidation of N-(p-bromobenzoyl)palytoxin with $NaIO_4$ on polystyrene gel column followed by separation gave an aldehyde (1), and two other aldehydes which were converted to alcohols (2) and (3), respectively by reduction. The aldehyde (1) was immediately treated with ethylene glycol and p-toluenesulfonic acid in benzene-1,2-dimethoxyethane under reflux to yield compound (4), which was converted to an acetate (5)[3] (m.p. 172-173°). The recrystallization of 5 from benzene gave well-formed and orthorhombic crystals. The space group is $P2_12_12_1$ and lattice constants are a= 17.31 Å, b= 28.76 Å and c= 5.166 Å. The structure was solved by using of MULTAN and refined to R= 8.0% by block-digonal least-squares method. A view of the molecule of compound (5) is shown in Fig.1.

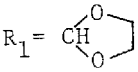
On the other hand, the alcohols (2) and (3) are the lipophilic segments obtained by oxidation followed by reduction with $NaBH_4$. Molecular formula of 3 is $C_{28}H_{54}O_6$,[4] and analysis of the PMR spectrum of its acetate (6) shows

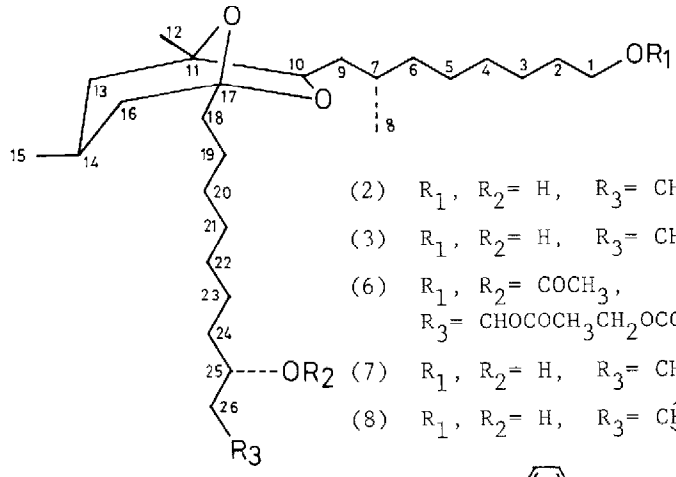
the presence of -CHOH-$CH_2$OH grouping in 3 [δ 5.29 (1H, m) and 4.10, 4.30 (1H each, ABX, $J_{AB}$= 12 Hz, $J_{AX}$= 4.0 Hz, $J_{BX}$= 6.0 Hz)]. Furthermore, in the CMR (20 MHz) spectrum of 6 the characteristic signal appeared at δ 107.5 as a singlet and this signal was originally observed at δ 108.8 as a singlet in the CMR (67.9 MHz) spectrum of palytoxin itself. This finding indicated that the quarternary carbon bearing two oxygens (C-17 in 6) is present in palytoxin itself. The tetraol (3) was expectedly converted to an aldehyde (7) [PMR (δ, $CDCl_3$) 4.17 (1H, m), 2.60 (2H, dd, J= 1.0 and 6.0 Hz) and 9.83 (1H, t, J= 1.0 Hz)] by the treatment with $NaIO_4$ in acetone-water. Compound (7) was reduced easily with $NaBH_4$ to give the triol (2). Furthermore, the aldehyde (7) was refluxed in benzene containing ethylene glycol and p-toluenesulfonic acid to give compound (8), which was transformed to the p-bromobenzoate (9) with p-bromobenzoyl chloride in pyridine at 50°. Recrystallization of 9 from hexane



(1) $R_1$= CHO, $R_2$= H

(4) $R_1$=  , $R_2$= H

(5) $R_1$=  , $R_3$= $COCH_3$

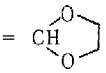


(2) $R_1$, $R_2$= H, $R_3$= $CH_2OH$

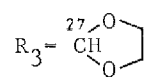
(3) $R_1$, $R_2$= H, $R_3$= $CHOHCH_2OH$

(6) $R_1$, $R_2$= $COCH_3$, $R_3$= $CHOCOCH_3CH_2OCOCH_3$

(7) $R_1$, $R_2$= H, $R_3$= CHO

(8) $R_1$, $R_2$= H, $R_3$= 

(9) $R_1$= CO-  -Br, $R_2$= H,

$R_3$= 

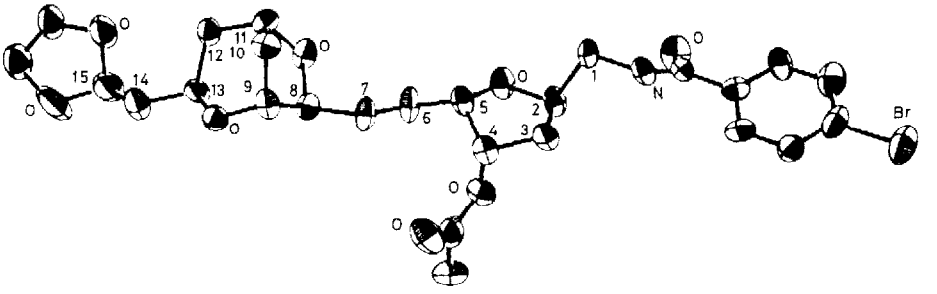



Fig.1. ORTEP drawing of the structure of 5 containing the terminal amino moiety of palytoxin.

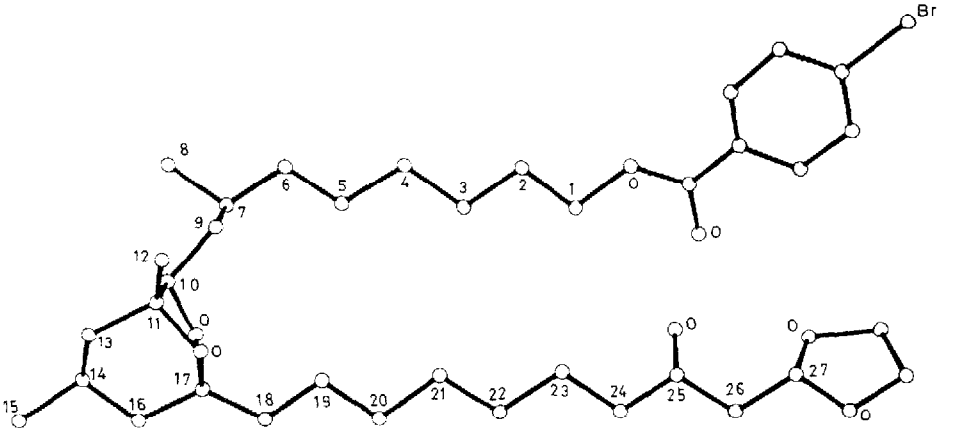



Fig.2. Molecular structure of compound (9) arising from the most lipophilic part of palytoxin.

afforded very fine crystals (m.p. 60-62°), which were further cut off to obtain the desirable single crystal (0.025 x 0.025 x 0.56 mm). The space group of 9 is C2 and lattice constants are a= 34.56 Å, b= 5.749 Å, c= 18.86 Å and β= 104.6° The structure was solved by using of MULTAN and refined by the block-diagonal least-squares method. The final R value was 10.4%. The computer-generated perspective drawing of the X-ray model of compound (9) is shown in Fig. 2.

Consequently, partial structures of palytoxin containing the terminal amino moiety and the most lipophilic part were clearly determined except for each absolute configuration which could be reported in the near future.

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## REFERENCES AND NOTES

1) Y. Hirata, D. Uemura, K. Ueda, and S. Takano, Pure Appl. Chem., 51, 1875 (1979).
2) D. Uemura, K. Ueda, Y. Hirata, C. Katayama, and J. Tanaka, Tetrahedron Lett., this issue.
3) The N-acetyl analog of compound (5) was obtained from N-acetylpalytoxin by the same chemical reactions as in the case of compound (5). Spectral data of this N-acetyl analog indicated that the molecular formula was $C_{21}H_{33}NO_8$ (m/e 427.2219, $M^+$), and there were seven methylenes and eight methine carbon atoms bearing one or two oxygen atoms as the carbon atoms originally present in palytoxin. This result was presented at the International Conference on Natural Substances of Biological Interest from the Pacific Area, Noumea, Nouvelle Caledonie, 1979.
4) It is found from its elementary analysis that crystalline 3 is assigned as a monohydrate (m.p. 99.5-101°).

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